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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/740,191	12/19/2000	Liang-Chang Dong	ARC 2556N1	7458

30766 7590 01/11/2005

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/740,191	DONG ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this c mmunication app ars on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-15,17,18 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-15,17,18 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Pri rity under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Request for Continued Examination (RCE) under 37 CFR 1.114 filed 09/21/04 and the Amendment and Applicant's Arguments/Remarks, both filed 08/16/04 is acknowledged.

Claims 12-15, 17, 18 and 24 are pending. Claims 12 and 17 have been amended. Claims 1-11, 16 and 19-23 have previously been cancelled. Claims 12-15, 17, 18 and 24 are rejected.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/16/04 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 12-15, 17, 18 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong *et al.* (US Pat. No. 5, 324,280).

Wong *et al.* teach an osmotic system for delivering a beneficial formulation to an environment of use wherein the osmotic system comprises: (a) a capsule; (b) a dosage amount of a beneficial agent liquid formulation; (c) an osmagent composition; (d) a semi-permeable composition; (e) at least one orifice that communicates with the exterior and the lumen wherein the osmotic system is delivered at a controlled rate. The formulation contains osmoagents (solutes), osmopolymers (hydrogels), various emulsions, oils, immiscible liquids, emulsifiers and the like (see reference col. 7, line 25 through col. 9, line 67); (col. 12, line 48 through col. 13, line 22) and claims.

The osmotic system comprises surfactants, selected from nonionic, anionic and cationic surfactants (col. 13, line 49 – col. 14, line 14). According to Wong *et al.*, the active drugs include steroids, hormonal agents, progesterone, nor-progesterone, drugs that act on hormone systems, reproductive systems and the like (col. 11, lines 40-60).

Wong *et al.* do not explicitly teach 'sustained release' of the dosage form, however they do teach that the osmotic systems release active agents at a *controlled* rate and over a prolonged period of time up to 24 hours (col. 2, lines 21-27 & 62-68). Furthermore, suitable rates of release (i.e., controlled, sustained, immediate) can be determined by one of ordinary skill in the art, through the use of routine or manipulative experimentation to obtain the best possible results.

Claims 12-15, 17, 18 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lambert *et al.* (US Pat. No. 6,458,373 B1) in view of Wong *et al.* (US Pat. No. 5,324,280).

Lambert *et al.* teach a self-emulsifying drug formulation system whereby the system is used for oral administration of water insoluble or poorly water-soluble drugs, wherein the oil phase with a surfactant and drug or drug mixture is encapsulated into soft or hard gelatin capsules (see reference column 3, lines 45-52); (col. 9, lines 36-55).

Lambert *et al.* teach that the composition includes alpha-tocopherol, a surfactant or mixtures of surfactants, with and without an aqueous phase, and a therapeutic agent, wherein the composition is in the form of a self-emulsifying drug delivery system. The pharmaceutical composition can be stabilized by various amphiphilic molecules, including anionic, nonionic, cationic, and zwitterionic surfactants (col. 3, lines 45-58).

The therapeutic agent can be any compound having natural or synthetic biological activity, is soluble in the oil phase, including peptides, non-peptides and nucleotides and lipid conjugates and prodrugs (col. 6, lines 49-55).

Lambert *et al.* teach that in the self-emulsifying formulation, the oil phase with a surfactant and drug or drug mixture is encapsulated into soft or hard gelatin capsules. Suitable solidification agents include high molecular weight polyethylene glycols and glycerides that can be added to allow filling of the formulation into a hard gelatin capsule at a high temperature. Semi-solid formulations are formed upon room temperature equilibration. Upon dissolution of the gelatin in the stomach and duodenum, the oil is released and forms a fine emulsion with droplets. The emulsion is then taken up in the intestine and released into the bloodstream (col. 9, lines 36-55).

The emulsion formulations comprise an array of surfactants and additives (col. 10, lines 5-27). The examples demonstrate various emulsion processes and their results (col. 10 through col. 23).

Lambert *et al.* are deficient only in the sense that they do not explicitly teach an expandable layer formed of an osmotic hydrogel and does not teach the capsule characteristics (inner surface, outer surface, semi-permeable membrane).

Wong et al. teach an osmotic system for delivering a beneficial agent formulation to an environment of use, wherein the osmotic system comprises hydrogels, also known as osmopolymers, and also teaches an inner capsule wall, an outer capsule wall and a semipermeable wall or membrane (see reference column 3, line 45 through col. 4, line 13); (col.8, line 48 through col. 9, line 25).

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Wong *et al.* within the teachings of Lambert *et al.*

because Wong *et al.* explicitly teach a drug delivery system comprising a capsule that contains the liquid drug formulation and various hydrogels, which serve to provide imbibition properties and swell in water and biological fluids and Lambert *et al.* teach a self-emulsification drug delivery system wherein the drug or drug mixture is encapsulated and filled into capsules. The expected result would be an improved and highly effective self-emulsification system for the delivery of therapeutic agents.

Prior Art made of record and deemed relevant by the Examiner:

Rudnic *et al.* US Pat. No. 5,897,876 (04/1999)

Response to Arguments

Applicant's arguments filed 08/16/04 have been fully considered but they are not persuasive.

Firstly, Applicant argued regarding the 35 U.S.C. §103(a) rejection of Claims 12-15, 17, 18 and 24 over Wong *et al.* (US 5,324,280) stating, "Wong *et al.* teach an osmotic dosage form wherein a drug formulation is contained within a capsule. The capsule itself is encapsulated within a hydro-activated layer. Thus, the interface between the drug formulation and the hydro-activated layer has a large surface area. For an oily drug formulation, significant mixing between the drug formulation and the hydro-activated layer when hydrated is not expected. However, if the drug formulation is self-emulsifying, there will be significant mixing between the drug formulation and the hydro-activated layer, which would lead to erratic release profile of the drug and a very high amount of drug residue after release. In contrast to the Wong *et al.*

system where the hydro-activated layer encapsulates the capsule containing the drug formulation, the surface area at the interface between the drug formulation and the expandable layer recited in claim 12 is small. This small surface area eliminates or minimizes undesirable mixing between the drug formulation and the expandable layer, especially after hydration."

These arguments have been fully considered, but were not found to be persuasive. Wong *et al.* teach a self-emulsifying osmotic drug delivery system wherein the hydro-activated layer imbibes and/or absorbs fluid into the drug emulsion layer. The osmotic system of Wong *et al.* comprises a similar structure as claimed, with the same active ingredients, such as progestogenic steroids, as claimed by Applicants. Also contained in Wong *et al.* are various surfactants, and surfactants are common emulsifiers known in the art. Moreover, features and characteristics argued by Applicant (*i.e*, space of interfaces, such as large, small) are not features or characteristics required by the claims. Even if, for sake of argument, such features with ranges were claimed, one of ordinary skill in the art could readily determine suitable ranges through the use of routine experimentation to obtain optimal results. Additionally, Wong et al. at column 2, lines 21-27, teach that the 'liquid formulation is initially essentially free of direct contact with a hydro-activated expansion composition, and which formulation can be delivered by the osmotic system at a controlled rate and continuously over a prolonged period of time'. Applicants argue that the instant claims provide for a 'self-emulsifying drug formulation and expandable layer contained within the same capsule, and that the expandable layer does not encapsulate the drug formulation'. However, Applicants have not demonstrated any unusual and/or unexpected results that accrue from this alleged structural distinction of a drug formulation and expandable layer contained within the same capsule in the first and second portions, respectively. The prior

art teaches effective delivery of therapeutic drugs over controlled periods of time and teaches the same components, used in the same field of endeavor, to treat the same problems, as that desired by Applicant. Thus, Applicant's arguments were not found persuasive.

Secondly, Applicant argued regarding the 35 U.S.C. §103(a) rejection of Claims 12-15, 17, 18 and 24 over Lambert *et al.* (US 6,458,373) in view of Wong *et al.* (US 5,324,280) stating, "Lambert *et al.* do not disclose that an expandable layer is also contained within the capsule. In contrast, claim 12 recites a self-emulsifying drug formulation and an expandable layer contained within the same capsule. This allows controlled release of the drug as well as minimizes undesirable mixing between the drug formulation and the expandable layer. Wong *et al.* fail to overcome the deficiencies of Lambert *et al.*"

These arguments have been fully considered, but were not found to be persuasive. Lambert *et al.* teach a self-emulsifying drug formulation system whereby the system is used for oral administration of water insoluble or poorly water-soluble drugs, wherein the oil phase with a surfactant and drug or drug mixture is encapsulated into soft or hard gelatin capsules. Lambert *et al.* do not expressly teach an expandable layer formed of an osmotic hydrogel. Wong *et al.* resolves this deficiency of Lambert *et al.* by teaching an osmotic system for delivering a beneficial agent formulation to an environment of use, wherein the osmotic system comprises hydrogels. The osmotic system of Wong *et al.* also comprises an inner capsule wall, an outer capsule wall and a semipermeable wall or membrane. Therefore, Lambert *et al.* in combination with Wong *et al.* renders the instant invention obvious. Applicant's arguments directed to 'controlled release' and mixing properties is not persuasive because the prior art teaches the delivery of drug in controlled and continuous release rates over time. The art also teaches that

the 'liquid formulation is initially essentially free of direct contact with a hydro-activated expansion composition'. By this teaching of the prior art, one would expect a minimum mixing action between the drug formulation and the expandable layer, as desired by Applicants. Furthermore, one of ordinary skill in this art would be well aware of the interaction required between ingredients or layers, to prevent adverse effects. Moreover, the Applicants, as delineated above, have not demonstrated any criticality in the positioning of the drug and expandable layers. The prior art teaches effective delivery of therapeutic progestogenic agents to an individual in need. Based on the reasons advanced above, the instant invention is rendered obvious and unpatentable over the cited art of record.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

H. N. Sheikh

Patent Examiner

Art Unit 1615

January 07, 2005

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